

b.) Amendments to the Claims

1. (Currently Amended) A method for inducing differentiation of an embryonic stem cell into an ectodermal cell, which comprises culturing the embryonic stem cell under non-aggregation conditions, wherein said culturing is carried out in the absence of retinoic acid.

2. (Currently Amended) The method according to claim 1, wherein the ectodermal cell is a cell ~~capable of differentiating~~ which differentiates into a nervous system cell or an epidermal system cell.

Claims 3-11 (Cancelled).

12. (Currently Amended) The method according to ~~any one of~~ claims 1 to ~~11~~, wherein said culturing is carried out in the presence of bone morphogenetic protein 4.

13. (Currently Amended) The method according to ~~any one of~~ claims 1 to ~~12~~, wherein said culturing is carried out in the presence of sonic hedgehog.

14. (Currently Amended) The method according to ~~any one of~~ claims 1 to ~~13~~, wherein the non-aggregation conditions are conditions not mediating an embryoid body.

15. (Currently Amended) The method according to ~~any one of~~ claims 1 to ~~14~~, which further comprises culturing under serum-free culture conditions.

16. (Currently Amended) The method according to ~~any one of~~ claims 1 to 15, wherein said culturing is carried out in the presence of a stroma cell-derived factor.

17. (Currently Amended) The method according to ~~any one of~~ claims 1 to 16, wherein said culturing is carried out in the presence of a stroma cell.

18. (Original) The method according to claim 17, wherein the stroma cell is a stroma cell whose proliferation potency is deleted by a physicochemical treatment.

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19. (Currently Amended) The method according to claim 18, wherein the physicochemical treatment is selected from the group consisting of ~~the following (a), (b) and (c):~~

(a) ~~a treatment with~~ an antitumor agent; (b) ~~a treatment by an~~ radiation irradiation; and (c) ~~a pathologic tissue fixative on used in pathologic diagnosis.~~

20. (Currently Amended) The method according to claim 19, wherein the physiocochemical treatment is an antitumor agent is selected from the group consisting of mitomycin C, 5-fluorouracil, adriamycin and methotrexate.

21. (Currently Amended) The method according to claim 19, wherein the physiocochemical treatment ~~for tissue fixation used in pathologic diagnosis~~ is selected from the group consisting of a microwave fixation, a rapid freeze-substitution fixation, a glutaraldehyde fixation, a p-formaldehyde fixation, a formalin fixation, an acetone fixation, a Van fixation, a periodic acid fixation, a methanol fixation and an osmic acid fixation.

22. (Currently Amended) The method according to ~~any one of~~ claims 16 to 21, wherein the stroma cell is recognized by a monoclonal antibody produced by a hybridoma FERM BP-7573.

23. (Currently Amended) The method according to ~~any one of~~ claims 16 to 22, wherein the stroma cell is selected from the group consisting of ~~the following (a), (b), (c), (d), (e), (f) and (g)~~: (a) a fetal primary culture fibroblast; ~~(b)~~ an SIHM mouse-derived STO cell; ~~(c)~~ a mouse fetus-derived NIH/3T3 cell; ~~(d)~~ an M-CSF deficient mouse calvaria-derived OP9 cell; ~~(e)~~ a mouse calvaria-derived MC3T3-G2/PA6 cell; ~~(f)~~ an embryonic stem cell-derived stroma cell; and (g) a bone marrow mesenchymal stem cell-derived stroma cell.

24. (Currently Amended) The method according to ~~any one of~~ claims 1 to 23, wherein the embryonic stem cell is selected from the group consisting of ~~the following (a), (b) and (c)~~:

- (a) an embryonic stem cell established by culturing an early embryo before implantation;
- (b) an embryonic stem cell established by culturing an early embryo produced by nuclear transplantation of the nucleus of a somatic cell; and
- (c) an embryonic stem cell in which a gene on the chromosome of the embryonic stem cell of (a) or (b) is modified using a gene engineering technique.

25. (Canceled)

26. (Currently Amended) The method according to ~~any one of~~ claims 1 to 25, wherein the embryonic stem cell ~~is differentiated~~ into an ectodermal cell or an ectoderm-derived cell at an efficiency of 5% or more.

27. (Currently Amended) The method according to ~~any one of~~ claims 1 to 26, which does not substantially accompany differentiation induction of a mesodermal system cell.

Claims 28-55 (Cancelled)

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56. (Currently Amended) A method for evaluating a substance for activity in relating to the regulation regulating in a differentiation step from of an embryonic stem cell into an ectodermal cell or an ectoderm-derived cell, which comprises:

carrying out the method according to any one of claims 1, 2 or 12 to 27 (i) in the presence of a substance to be tested and ~~the method~~ (ii) in the absence of the substance to be tested; and

comparing ~~the differentiation step from an of the~~ embryonic stem cell into an ectodermal cell ~~or an ectoderm-derived cell~~ obtained in the presence of the substance to be tested with that in the absence of the substance to be tested.

57. (Currently Amended) A method for screening a substance for activity in relating to the regulation regulating in a differentiation step from of an embryonic stem cell into an ectodermal cell ~~or an ectoderm-derived cell~~, which comprises:

carrying out the method according to any one of claims 1, 2 or 12 to
27 (i) in the presence of a substance to be tested and ~~the method~~ (ii) in the absence of the
substance to be tested; and

comparing ~~the differentiation step from an~~ of the embryonic stem
cell into an ectodermal cell ~~or an ectoderm-derived cell~~ obtained in the presence of a
substance to be tested with that in the absence of the substance to be tested.

Claims 58-71 (Cancelled).
